IN THE SPECIFICATION:

Please amend the specification as follows.

Please replace the first paragraph, lines 1-2, on page 45 with the following paragraph:

Example 2. SPECIFIC CHANGES IN INTRACELLULAR CALCIUM CONCENTRATIONS INDUCED IN ~~CHOG-16-IGS4~~ CHOGα16-IGS4 CELLS BY NEUROMEDIN U.

Please replace the third paragraph, lines 6-11, on page 45 with the following paragraph:

A. Method and Materials for IGS-4 transfected ~~CHOG-16-cells~~ CHOGα16-IGS4 cells.

The following materials were used in the experiments: Vector containing IGS4-DNA sequence (IGS4-pcDNA3.1); SuperFect Transfection Reagent (Qiagen); Nut-Mix F12 (Gibco) with 10% FCS, 0.028mg/ml Gentamycin (Gibco); 0.22mg/ml Hygromycin (Gibco).

Materials used for clone selection: Nut-Mix F12 with 10% FCS; 0.028mg/ml Genatmycin; 0.22mg/ml Hygromycin and 0.55mg/ml Geneticin (Gibco).

Please replace the paragraph bridging page 46, line 37, and page 47, line 8, with the following paragraph:

To identify the endogenous ligand for the orphan G protein coupled receptor (GPCR) IGS4, IGS4 (both forms IGS4A and IGS4B) was stably transfected in Chinese Hamster Ovary (CHO) cells. Since the G protein coupling mechanism of IGS4 was unknown, a

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1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

specific CHO-cell strain was used. These CHO-cells stable express the G-protein ~~G 16~~ Gα16 (~~CHOG 16~~ CHOGα16, Molecular Devices), which is known as "universal adapter" for GPCRs (Milligan G., Marshall F. and Rees S. (1996), Gα16 as a universal G protein adapter:.implications for agonist screening strategies. *TIPS* 17:235-237).

The resulting ~~CHOG 16-IGS4~~ CHOGα16-IGS4 cells were functionally screened on a Fluorometric Imaging Plate Reader (FLIPR) to measure mobilisation of intracellular calcium in response to putative ligands. At the concentration of 10nM neuromedin U-23 induced a large, transient and robust calcium-response. In contrast, ~~CHOG 16~~ CHOGα16 cells and ~~CHOG 16~~ CHOGα16 cells expressing another, unrelated orphan GPCR, did not respond to neuromedin U-23. The results of these experiments with IGS4B are shown in Fig. 4.

Please replace the third full paragraph on page 47, lines 25-28, with the following paragraph:

The calcium mobilization response seen following activation of IGS4 by neuromedin U suggests that this receptor is coupled to G proteins of the Gq/11 subfamily, In addition, basal levels of intracellular camp were not modulated by porcine neuromedin U-8 (1 and 10μM) in ~~CHOG 16-IGS4~~ CHOGα16-IGS4 cells, suggesting that this receptor does not couple to G proteins of the Gs subfamilies (data not shown).

Please replace the last paragraph on page 52, lines 32-38, with the following paragraph:

Fig.3: IGS4 receptor activation by different Neuromedin U isoforms. ~~CHOG 16-IGS4B~~ CHOGα16-IGS4B cells were cultured in 96-well plates overnight and loaded with Fluo-

FINNEGAN
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DUNNER LLP
1300 I Street, NW
Washington, DC 20005
202.408.4000
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4AM. The receptor mediated Ca^{2+} changes were measured with FLIPR (Molecular Devices). Maxima of the fluorescence change detected by the CCD camera were normalized to 1 and are depicted as counts.

Fig. 3a: results for neuromedin U-8;

Fig. 3b: results for neuromedin U-23;

Fig. 3c: results for neuromedin U-25.

Please replace the first paragraph on page 53, lines 1-5, with the following paragraph:

Fig.4 Neuromedin U-23 induced intracellular Ca^{2+} mobilization in ~~CHOG 16-cells~~ CHOGα16-cells expressing IGS4B. Application of 10nM Neuromedin U-23 to the cell lines ~~CHOG 16-IGS4~~ CHOGα16-IGS4, ~~CHOG 16~~ CHOGα16 and ~~CHOG 16~~ CHOGα16 transfected with an other orphan GPCR. Cells were cultured in 96-well plates overnight and located with Fluo-4AM. Receptor mediated intracellular Ca^{2+} changes were measured with FLIPR (Molecular Devices), depicted in counts detected by the CCD camera.

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HENDERSON
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DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
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